

using a 1165PR stripper with an ultrasonic vibrator for approximately 100 min at 95° C. Finally, the magnetic islands were magnetized along the x-axis using a vibration sample magnetometer (VSM) at 9000 Gauss to ensure saturation of the magnetic islands.

[0206] (2) A chip was fabricated on a wafer of silicon essentially as described above except that optical lithography was used rather than e-beam lithography, using visible light to form the mask patterns. An image of the entire wafer (magnetic chip) is shown in **FIG. 9**. The wafer contains an array of arrays at a spacing of approximately 0.1 inch in each direction. Each spot which is visible is itself a microarray of magnetic islands (shown at greater magnification in **FIGS. 6 and 11**) in a 30×30 configuration, with an island-to-island spacing of approximately 30 μm in both the x and y directions. The wafer therefore contains approximately 900 sites per subarray and well over 500 such subarrays. An experiment involving the analysis of 100 genomic markers on each of 500 individuals could be performed in one run on this wafer (assuming 9-fold redundancy).

Example 2

Assembling a Random Array of Magnetic Beads on a Magnetic Chip

[0207] A magnetic chip was fabricated essentially as described in Example 1 except that (i) the mask was designed to produce a chip with a 10×10 array of arrays, with each subarray having a 30×30 configuration of magnetic islands; (ii) the magnetic islands were diamond-shaped rather than rectangular and had an island-to-island spacing of approximately 20 μm in both the x- and y-dimensions, and (iii) the etching time was varied across the chip in the x-dimension, resulting in a gap of variable width, ranging between 1 and 4 μm .

[0208] A stock solution of superparamagnetic beads (streptavidin-conjugated M-280 Dynabeads obtained from Dynal Biotech, Inc.) was washed with buffer according to the directions of the manufacturer and labeled with biotinylated fluorescent R-phycoerythrin dye (Molecular Probes, Inc.) also according to the directions of the manufacturer. The beads were diluted at 40:1 in 1×TE (Tris-EDTA) with 0.1% SDS, yielding a concentration of approximately 17,000 beads/ μl . A 10 μl drop of the labeled bead solution was applied to the magnetic chip with a Pasteur pipette, and the beads were allowed to become trapped by the localized magnetic fields at room temperature for approximately 5-10 minutes. The remaining solution was drained off the chip. The chip was then scanned for fluorescence in a confocal array laser scanner (excitation at 488 nm, fluorescence at 570 nm) to visualize the beads on the array. A fast fluid flow (1 m/sec) was used to remove the beads from the chip after detection.

[0209] **FIG. 8** shows the laser-induced 570 nm fluorescence scan of the entire chip with a random array generated as described above. The overall pattern of the 10×10 array of arrays is clearly visible. The inset shows an enlarged view of one of these subarrays, containing a 30×30 pattern of magnetic regions. The vertical scale in the image is 20 $\mu\text{m}/\text{count}$. Thus the inset shows a section of the chip 70

counts=1400 μm in length. The arraying of the magnetic beads in a grid-like pattern is clearly visible. The current resolution is 10 mm per pixel in the vertical direction. Since the magnetic regions are spaced 20 mm apart, bead trapping can be seen on every other line. (The very faint spots next to bright ones in the image are an artifact of the overall resolution of the laser scanner. A factor of two improvement in the resolution would eliminate this artifact.)

[0210] The effect of gap width on the arraying behavior of the magnetic beads is clearly visible in **FIG. 8**. The right side of the figure shows subarrays having a gap width of approximately 1 mm, which resulted in a low trapping efficiency. The trapping efficiency increased as the gap width increased (from right to left across the image). The maximum trapping efficiency occurred at a gap width approximately the same as the diameter of the beads (3 μm). A lower trapping efficiency was observed with a gap width greater than the bead diameter (left side of image). In addition, the increased gap width resulted in trapping of multiple beads at some locations.

Example 3

Detecting DNA Hybridization Using a Random Array of Magnetic Beads

[0211] A stock solution of superparamagnetic streptavidin-conjugated M-280 Dynal beads (10 mg/ml) was cleaned thrice following the manufacturer's directions. The stock beads are specified to bind up to 20 pmole of biotinylated oligo per 10 μl of stock beads. We cleaned 10 μl of stock beads and diluted them 2-fold to 20 μl . 200 pm of biotinylated oligo (2 μl of 100 pm/ μl) was then added and bound to the bead for 30 minutes at 40° C. while shaking on an Eppendorf Thermomixer. 1M NaCl salt buffer conditions were used, in accordance to the manufacturer's protocols. A ten fold excess of biotinylated oligo was used to saturate all the available binding sites on the bead. The oligo sequence used was 5'-[BiotinTEG]TTT TTT ACT GGC CGT CGT TTT ACA-3'. The six T's closest to the 5' end were inserted to form a linker for the 18-mer oligo. These may not be necessary.

[0212] The beads were then captured (magnetically) and excess oligo removed by washing three times with the same 1M buffer and resuspended into 100 μl (corresponding to a 10-fold diluted bead density compared to the original stock). A 40 μl batch of beads was incubated for 20 minutes at 45° C. with complementary oligo labeled with Cy3 dye (at a concentration of 1 μM). The sequence of the oligo is 5'-Cy3-TGT AAA ACG ACG GCC AGT-3'. Again, 1M NaCl conditions were used. The beads were then washed thrice to remove excess labeled oligo and resuspended in 1×TE with 0.001% TWEEN. The sample was arrayed as described in Example 2, on a magnetic chip with islands at a spacing of 20 μm in each direction.

[0213] A confocal fluorescence scan of the chip was performed at 488 nm excitation (using an argon laser) and signal collected at 570 nm. **FIG. 13** shows a fluorescence image of a 30×30 array obtained from this experiment. The image was obtained using a 50× objective with a photomultiplier tube at low setting with a 570 nm centered optical bandpass filter. The scale of the image is 5 $\mu\text{m}/\text{count}$; thus the size of the array is approximately 0.6 mm on each side.